

REPORT 4834/R

**CIPAC FULL SCALE COLLABORATIVE STUDY ON THE DETERMINATION OF CYAZOFAMID
IN CYAZOFAMID TECHNICAL MATERIAL AND FORMULATED PRODUCT
BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY**

Progress Report to CIPAC on Method Development Work
Conducted by the ISK Company

By

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1 INTRODUCTION

The results of CIPAC full scale collaborative study for Cyazofamid technical product and Cyazofamid suspension concentrate are reported in this present study for its content of Cyazofamid.

In October 2011, CIPAC Information Sheet No. 291 was sent out by the CIPAC Secretary inviting members to participate in a collaborative study to validate the high performance liquid chromatographic assay method for cyazofamid in technical material and formulated product. A copy of the analytical method, protocol for the performance of the study, analysis report forms, samples and standards required for the analysis were sent to the respondents. The participants who completed the study are listed in Section 1.2.

The analytical method assessed in this study took into consideration CIPAC comments made in the frame of the small scale collaborative trial (report presented in June 2011).

1.1 Samples

Five test samples, homogenized, and analytical standards were sent to the participants. All samples came from different batches of technical material and formulation.

Test Sample	Identification Code
Cyazofamid Technical batch 9506	Tech-1
Cyazofamid Technical batch 9801-2	Tech-2
Cyazofamid 400 SC batch 310990	Cyazofamid 400 SC-1
Cyazofamid 400 SC batch 311614	Cyazofamid 400 SC-2
Cyazofamid 400 SC batch 311698	Cyazofamid 400 SC-3

Cyazofamid analytical standard (batch No. Y-UD-111031, 99.7 % purity) were provided by ISK.

1.2 Participants

Lab 1	Fabian Etienne-Thewissen	AFSCA Rue Louis Boumal,5 4000 LIEGE Belgium
Lab 2	Vanessa Lecocq	Walloon Agricultural Research Centre (CRA-W) Agriculture and Natural Environment Department (D3) Plant Protection Products and Biocides Physico-chemistry and Residues Unit (U10) Carson Building Rue du Bordia, 11 B - 5030 - GEMBLoux Belgium

Lab 3	Bruno Patrian	Agroscope Changins-Wädenswil ACW Plant Protection Chemistry Schloss 1 CH-8820 Wädenswil Switzerland
Lab 4	Xiangdong Shao	Nutrachim Laboratory Co., Ltd. D-1, Dongsheng Science Park, 66 Xixiaokou Road, Haidian District, Beijing 100192 P. R. China
Lab 5	Michael Haustein	CURRENTA GmbH & Co. OHG ANT Produktionsanalytik Building A 559 D-41538 Dormagen Germany
Lab 6	Luis Manso	Laboratorio Arbitral Agroalimentario. Ministerio de Agricultura, Alimentación y Medio Ambiente Aguarón, 13. Aravaca. 28023 Madrid Spain
Lab 7	Lajos Benke	National Food Chain Safety Office, Directorate of Plant Protection Soil Conservation and Agri-environment, Pesticide Analytical Laboratory Ország út 23 H-2481 Velence Hungary
Lab 8	Dewi Lesmawaty	PT Agricon JL. Melati No.5 Desa Wanaherang Kec. Gunung Putri. Cibinong, 16965 Indonesia
Lab 9	Jim Garvey	Pesticides Control Service Laboratory Department of Agriculture, Food and the Marine, Backweston Campus, Youngs Cross, Celbridge, Co. Kildare IRELAND
Lab 10	Krste Tashev	State Phytosanitary Laboratory Ministry of Agriculture, Forestry and Water Economy bul Aleksandar the Great bb, 1000 Skopje (SPL) Jurij Gagarin br. 15 1000 Skopje (MAFWE) REPUBLIC OF MACEDONIA

Lab 11	Brenda Checa	Quality Control of Pesticides Formulation Laboratory Tocumen Rio Tapia PANAMA
Lab 12	Florentina Nedelcu	Central Phytosanitary Laboratory 11 Voluntari St, Code 077190, Voluntari Romania
Lab 13	Ana Gregorčič	AGRICULTURAL INSTITUTE OF SLOVENIA (Kmetijski inštitut Slovenije) Hacquetova ulica 17, 1000 Ljubljana, SLOVENIJA
Lab 14	Juliana Schlosserova	Central Controlling and Testing Institute in Agriculture (ÚKSÚP) Hanulova 9/A, 844 29 Bratislava 42 Slovakia
Lab 15	Andrew Plumb	The Food and Environment Research Agency Sand Hutton, York, North Yorkshire YO41 1LZ, UK

2 ANALYTICAL METHOD

2.1 Scope

This method is applicable to the determination of Cyazofamid in Cyazofamid technical (i.e. Technical Grade Active Ingredient or TGA). This method is also applicable to the determination of Cyazofamid in the formulation Cyazofamid 400 SC.

2.2 Outline of method

Cyazofamid is determined in the test samples by reversed-phase high performance liquid chromatography using ultraviolet detection at 280 nm. Quantification is done by external standardization.

2.3 Procedure

Each sample was analyzed by four independent determinations ($n_i = 4$). The samples were analyzed in a first run (Day 1) by duplicate injections of two weighings for each sample. The sequence was repeated on a second date (Day 2) with two other weighings of each sample. The Cyazofamid content for each injection was calculated using the mean response factor from the calibration solutions bracketing the injections of the sample solutions (single point calibration). For the calculation of the content of a sample, the mean value of the duplicate injections was used. For further details, please see attached full method description.

3 REMARKS OF PARTICIPANTS**3.1 Analytical Conditions**

Lab	Liquid chromatograph; Detector; Injector	Column	Mobile phase ⁽¹⁾	T (°C)	Flow (ml/min)	Vol inj (µl)
1	Varian 9050; Automatic, Varian ProStar	Luna C18(2) 100A; 150mm x 4.6mm x 5µm; 529946-4	H2O pH4 with Hac/ ACN/ CH3OH : 43/32/25	40	1.2	5 (D1) 10 (D2)
2	Waters Alliance 2695 Separation Module; Waters 996 PAD; Automatic	Phenomenex SphereClone ODS-2, 5 µm, 250 x 4.6 mm i.d.; Serial No. 565563-2	water (pH 4 with acetic acid) - acetonitrile - methanol (43-32-25 v/v)	40	1	5
3	Dionex Summit; Diodenarray detector, Dionex PDA-100; Automatic, CTC LC-PAL	Inertsil ODS2 5um 4.6mmx250mm	Water (pH 4 with acetic acid)- acetonitrile-methanol (43-32-25 v/v)	40	1	10
4	Agilent HPLC 1200 system fitted with DAD	BDS HYPERSIL C18 (Thermo, 4.6mm*250mm*5um, 1181402M)	Water[pH=4.0 HAC]: Acetonitrile: Methanol=43:32:25	40	1	Auto-matic
5	Agilent 1260 DAD; Automatic	Agilent Technologies ZORBAX Eclipse XDB-C18, 4,6*250mm, 5µm; Serial-No.: USNH005742	43% demin. Water (pH 4 with acetic acid) + 32% acetonitrile + 25% methanol (v/v/v)	40	1	5
6	Agilent 1100; Automatic	Phenomenex Luna C18(2) 100A (250x4,6mm); Serial No. 382218-8	Acetonitrile/Methanol /Water pH 4,0 (32:25:43)	40	1	5
7	Dionex, UVD 170S; Automatic, Dionex ASI 100	Agilent, Zorbax SB-C18, 4,6x250mm, 5µm, USCL 020208	H2O(pH4)/CH3CN/CH 3OH 43/32/25	25	0.8	5
8	SHIMADZU 20 AD; UV, SPD-20A; Manual	Phenomenex Luna 5 µ C18 (2) 100 A, 250 x 4.6 mm (i.d), C18, particle size 5 µm; S/No : 608806-27	Water (pH with acetic acid) – Acetonitrile – Methanol (43-32-25 v/v)	40	1	10
9	AGILENT 1100 SERIES; DAD – G1315B; Automatic – G1313A	SPHERECLONE – PHENOMENEX – 250 X 4.6mm 5um; 565016-1	H2O(Ph 4 with Acetic Acid):Acetonitrile:Met hanol (43:32:25 v/v)	40	1	5

10	VARIAN Pro Star, pump 230, auto-sampler 430, column thermostat 550; PDA Detector VARIAN 330	VARIAN 250mm length, 4.6 mm internal diameter, 5µm particle size, Microsorb 100 C18; Serial No: 279183	Water (pH 4 with acetic acid)-acetonitrile-methanol (43-32-25 v/v)	40	1	5
11	HPLC 1100; DAD, Agilent G1315B; Automatic injector, G1313A ALS	Agilent Zorbax ODS (4.6 x 250 mm) 5 micron non endcapped; Serial No.884950-543	water (pH 4 with acetic acid) acetonitrile-methanol (43-32-25 v/v)	40	1	5
12	VARIAN PROSTAR 345; Automatic, VARIAN PROSTAR 410	Phenomenex SphereClone 5u ODS (2) 250x4.6mm; S/N:603181-4	Water (Ph 4 with acetic acid)-acetonitril-methanol (43-32-25 v/v)	40	1	5
13	Agilent 1200 Series; Diode Array Detector SL G1315D; Auto-sampler G1367B	Lichrospher 100 RP-18, 4.6 mm i.d. x 250 mm, 5 µm; serial No.: 029823	water (pH 4 with acetic acid) : acetonitrile : methanol = 43 : 32 : 25 (v/v)	40	1	5
14	HPLC Agilent 1100 Series ; VWD; Autosampler	Zorbax Extend-C18, 4.6x250 mm, 5µm 80A; S.No.: USHR002941	Water pH4 (with acetic acid):acetonitrile:met hanol (43:32:25)	40	1	5
15	Hewlett Packard 1050 ; 1090 DAD; Automatic	250 x 4.6 mm Sphereclone ODS2 5µm (Phenomenex); s/n 454405-1	water (pH 4 with acetic acid) - acetonitrile - methanol (43-32-25 v/v)	40	1	5

T = Temperature Vol inj = Volume injected

⁽¹⁾ Isocratic conditions

3.2 Remarks

Several labs made comments about the performance of the method and noted deviations from the method that occurred:

Lab 1 No comments.

Lab 2 For chromatograms of sample solutions, there was an interference at the beginning of cyazofamid peak.

The volumetric flasks were filled up to volume at 20°C ± 1°C instead of at room temperature. Technical solutions were filtered on 0.45 µm PTFE filters.

Lab 3 We found the method quite straightforward and easy to carry out.

We feel that the retention time of cyazofamid is excessively long (23 min in method, in our analysis system approx. 27 min). Consequently the runtime with 45 min is quite long as well. We wonder whether the retention time is needed for separation of coeluting compounds.

- Lab 4 Only CYAZOFAMID 400 SC and CYAZOFAMID standard were shipped to our Lab. We did not receive the CYAZOFAMID Tech samples. We only analyse 3 batches CYAZOFAMID 400 SC samples.
CYAZOFAMID 400 SC samples cannot be dissolved completely after sonicating for 5 minutes. A little bit of samples still left after sonicating for 10 minutes. The results in Excel were obtained after 30 minutes sonication. Actually, we did analyse the samples after sonicating for 10 minutes, and the results were much lower than the results reported in the excel spreadsheet.
- Lab 5 Technical samples were also filtered by Chromafil Xtra. Type of Integrator: DIONEX Chromeleon. Used 0,45µm-filters: Chromafil Xtra, Macherey&Nagel, RC 45/25
Ret.Time: Day 1 approx. 20 min. instead of 23 min. Day 2 approx. 23 min.
PeakPurity checked.
In Sheet 'Summary' Cell D7 corrected to 'day1;G33'.
- Lab 6 Sample concentration has been reduced to minimize possible interferences and to get better information of the peak purity with the UV spectrum.
2 mL of water have been added to the SC samples to improve AI extraction.
- Lab 7 No comments.
- Lab 8 Area sample and standard calculated with this method stable at retention time approx. 33-34 minutes. This result is different from the reference method CIPAC (retention time is approx. 23 min). All the method and HPLC condition same with the reference method. Time for sonicate sample until sample complete dissolve need time more than 15 minutes. Our laboratory need 1 hour to get sample complete dissolved. We used sonicator Restch.
- Lab 9 No comments and deviations. The analysis went well.
- Lab 10 Preparing of the standards and samples was very easy and was not time consuming. Proposed time for sonication of the samples was not sufficient, I used for all 3 samples 2 x 5 min, and shaking between. General the test method is very nice and user friendly. I have earlier ret. time and it was approximately at 20.9 min.
The chromatography system that we have it's relatively new, but we do not have UPS that will make constant current during performing the analysis. Because of the long total analysis time approximate 24 hours for conditioning of the system and analysis, and having change in the current quality during the day and night, we do not have very constant response factor f_i especially on the Day 2, when I have also and power cut off at the last sample (3a and 3b) as you can see from the EXCEL data sheet, and I have to repeat the sequence.
- Lab 11 We had a good performance in the time of preparation of reference materials and samples in normal conditions, however if we had had any inconvenient additional with our LC; the analysis delayed more time to deliver of the results because the time of chromatography is very long.
The method is selective, but the injection time was very long. Approximately 20 hours which demands a lot of mobile phase where analysis of a significant volume of samples with this active ingredient.
The retention time varied significantly up (30 min) according to the seted in the method (23 min).

Lab 12 I weighted about 40 mg of cyazofamid reference standard instead of 85 mg

Lab 13 No comments.

Lab 14 For preparation of calibration/sample solution were used 25 ml volumetric flasks, maintaining the prescribed final concentration.

Lab 15 Retention time of cyazofamid is shorter (18.1 mins) than approx. time given in method (23 mins). Did not feel it was necessary to adjust mobile phase/flow rate to obtain a closer match. Overall run time shortened to 40 minutes. Response factors for day 2 are slightly higher than day 1, therefore overall results are slightly higher.
Small co-eluting peak observed in technical material samples.

4 RESULTS AND DISCUSSION

The statistical evaluation of the collaborative trial was performed according to DIN ISO 5725. Samples were sent to 15 laboratories. All laboratories sent back results and the results reported by the participants were all used. Lab 4 only determined the content of Cyazofamid in formulation samples and consequently was included only for evaluation of those data. The assay results reported by the laboratories are listed in Tables 2-6, and are presented in Figures 1-5.

Statistical evaluation of the data was done following “Guidelines for CIPAC Collaborative Study Procedures for Assessment of Performance of Analytical Methods.” The data were examined for outliers and stragglers using Cochran’s test on the within-lab variability, followed by Grubbs-I on the laboratory means, and iterating where necessary. Where deemed necessary, an additional Grubbs-II test was conducted to identify two stragglers or outliers. The tests were performed at an alpha level of 0.01 for outlier, and 0.05 for straggler. Based on this procedure, the Cochran and Grubbs-I tests identified the following potential outlier and straggler lab data from the sample sets. Straggler and outlier values are reported below.

Cyazofamid determination				
Code Sample	Cochran Straggler	Cochran Outlier	Grubbs-I Straggler	Grubbs-I Outlier
Tech-1	none	none	none	none
Tech-2	none	none	none	none
Cyazofamid 400 SC - 1	none	Lab 10	none	Lab 10
Cyazofamid 400 SC - 2	none	Lab 8	Lab 8	none
Cyazofamid 400 SC - 3	none	Lab 9,10	none	Lab 10

A summary of the statistical evaluation for the labs is given in Table 1, which includes the repeatability and reproducibility values, as well as the between-lab experimental Reproducibility Relative Standard Deviation, %RSD_R and the calculated acceptable value, %RSD_{R(Hor)}, based on the Horwitz curve calculation.

4.1 Cyazofamid

Tech-1

No straggler or outlier was detected by the Cochran test of variance homogeneity. Variance from Lab 8 and Lab 10 were significantly higher than for the other labs, and were only not detected by the Cochran test because they occurred at the same level ($s_i = 11.1$ and 11.0). As the average values were still acceptable the values were maintained. Grubbs-I for all labs did not identify a straggler or outlier (nor did Grubbs-II).

The statistical analysis of these results show the Repeatability Relative Standard Deviation (%RSD_r) and the between-lab Reproducibility Relative Standard Deviation (%RSD_R) for the determination of Cyazofamid in Cyazofamid technical 1 sample to be well below the limit calculated (%RSD_{R(Hor)}) using the Horwitz equation.

Tech-2

No outlier or straggler was detected by the Cochran test of variance homogeneity. Variance from Lab 2 and Lab 10 were significantly higher than for the other labs, and were only not detected by the Cochran test because they occurred at about the same level ($s_i = 7.8$ and 8.1). As the average values were still acceptable the values were maintained. Grubbs-I for all labs did not identify a straggler or outlier (nor did Grubbs-II).

The statistical analysis of these results show the Repeatability Relative Standard Deviation (%RSD_r) and the between-lab Reproducibility Relative Standard Deviation (%RSD_R) for the determination of Cyazofamid in Cyazofamid technical 2 sample to be well below the limit calculated (%RSD_{R(Hor)}) using the Horwitz equation.

Cyazofamid 400 SC-1

An outlier was detected by the Cochran test of variance homogeneity for Lab 10. Variance from Lab 10 is the highest and the mean value at 358.9 g/kg was significantly higher than the others, which was detected also by the Grubbs-I test. In its comment the lab stated issues with keeping the response factor stable over the time for analysis. The lab 10 value is maintained in the statistical evaluation presented in Table 1A, but was removed for evaluation in the refined Table 1B. This refinement did not have a major impact on the observed overall mean value, but did improve significantly the Reproducibility parameter.

The statistical analysis of these results show the Repeatability Relative Standard Deviation (%RSD_r) and the between-lab Reproducibility Relative Standard Deviation (%RSD_R) for the determination of Cyazofamid in Cyazofamid 400 SC-1 sample to be well below the limit calculated (%RSD_{R(Hor)}) using the Horwitz equation, even before excluding lab 10.

Cyazofamid 400 SC-2

An outlier was detected by the Cochran test of variance homogeneity for Lab 8. Variance from Lab 8 is the highest and the mean value at 358.3 g/kg was significantly higher than the others, which was detected also by the Grubbs-I test. In its comment the lab stated issues with the sonication step and the need to extend time for dissolution, but this does not explain the obtained high mean value. The lab 8 value is maintained in the statistical evaluation presented in Table 1A, but was removed for evaluation in the refined Table 1B. This refinement did not have a major impact on the observed overall mean value, but did improve significantly the Reproducibility parameter.

The statistical analysis of these results show the Repeatability Relative Standard Deviation (%RSD_r) and the between-lab Reproducibility Relative Standard Deviation (%RSD_R) for the determination of Cyazofamid in Cyazofamid 400 SC-2 sample to be well below the limit calculated (%RSD_{R(Hor)}) using the Horwitz equation, even before excluding lab 8.

Cyazofamid 400 SC-3

Two outliers were detected by the Cochran test of variance homogeneity for Labs 9 and 10. Variance from Lab 10 is the highest and the mean value at 365.7 g/kg was significantly higher than the others, which was detected also by the Grubbs-I test. In its comment the lab stated issues with keeping the response factor stable over the time for analysis. The lab 10 value is maintained in the statistical evaluation presented in Table 1A, but was removed for evaluation in the refined Table 1B. Lab 9 value was maintained in both evaluations as the average value was still acceptable. This refinement did lower the observed overall mean value, and did improve significantly the Reproducibility parameter.

The statistical analysis of these results show the Repeatability Relative Standard Deviation (%RSD_r) and the between-lab Reproducibility Relative Standard Deviation (%RSD_R) for the determination of Cyazofamid in Cyazofamid 400 SC-3 sample to be well below the limit calculated (%RSD_{R(Hor)}) using the Horwitz equation, even before excluding lab 10.

5 CONCLUSION

After examination of all provided laboratory data and identification of stragglers and outliers, retention of all laboratory data was statistically valid for the determination of Cyazofamid in Cyazofamid technical. Labs 2, 8, and 10 showed high within-lab variability, but were not detected by the Cochran test. Although it led to somewhat higher repeatability and reproducibility, Horwitz criteria were met.

After examination of all provided laboratory data and identification of stragglers and outliers, retention of all laboratory data was statistically valid for the determination of Cyazofamid in Cyazofamid formulation. Nevertheless, a refinement was proposed after removal of outlier data from Lab 8 or 10 for the three formulation analyses. Removal of the outliers improved the statistical evaluation, especially for the Reproducibility parameter.

The between-lab Reproducibility Relative Standard Deviation (%RSD_R) and the Repeatability Relative Standard Deviation (%RSD_r) were well below the limit calculated (%RSD_{R(Hor)}) using the Horwitz equation for the determination of Cyazofamid in Cyazofamid technical and Cyazofamid formulation with no outlier removed. After removal of the outliers, the conclusion remains the same, i.e. %RSD_R and %RSD_r are still below %RSD_{R(Hor)}.

The acceptance of this method as an approved CIPAC assay method for Cyazofamid in Cyazofamid technical and Cyazofamid formulation is recommended.

ACKNOWLEDGEMENTS

ISK wishes to thank all the laboratories and their staff who participated in this study.

TABLES (1-6)

**TABLE 1A - Cyazofamid – Summary of the statistical evaluation of the collaborative Study Data
All Test Results Retained (No outlier removed)**

	Cyazofamid 400 SC				
	Tech-1	Tech-2	SC-1	SC-2	SC-3
No. of Labs	14	14	15	15	15
No. of Stragglers	0	0	0	1 ^(G)	0
No. of Outliers	0	0	1 ^(C,G)	1 ^(C)	2 ^(C,G)
No. of Labs Retained	14	14	15	15	15
No. of Results	56	56	60	60	60
Total Mean, X (g/kg)	958.7	948.7	346.3	346.8	343.4
Repeatability standard deviation S_r	5.51	4.38	2.76	3.52	3.71
“Pure” between laboratory standard variation S_L	5.48	4.20	4.02	3.74	6.45
Reproducibility standard deviation S_R	7.77	6.07	4.88	5.14	7.44
Repeatability r	15.4	12.3	7.73	9.86	10.4
Reproducibility within lab R_L	15.3	11.8	11.3	10.5	18.0
Reproducibility between labs R	21.8	17.0	13.7	14.4	20.8
RSD_r (%)	0.58	0.46	0.80	1.02	1.08
RSD_R (%)	0.81	0.64	1.41	1.48	2.17
RSD_{R(Hor)} (%)	2.01	2.02	2.35	2.35	2.35

Limits (g/kg)

X+R	980.4	965.7	360.0	361.2	364.2
X+r	974.1	960.9	354.1	356.6	353.8
X-r	943.2	936.4	338.6	336.9	333.0
X-R	936.9	931.7	332.7	332.4	322.6

^(C) from Cochran test

^(G) from Grubbs-I test

Where :

X = average

S_r = repeatability standard deviation

S_L = “pure” between laboratory standard deviation

S_R = reproducibility standard deviation = $(S_r^2 + S_L^2)^{0.5}$

r = repeatability within-lab (2.8 S_r)

R = reproducibility between labs (2.8 S_R)

R_L = reproducibility within lab on different days (2.8 S_L)

% RSD_r = repeatability relative standard deviation (100 S_r/X)

% RSD_R = reproducibility relative standard deviation between labs (100 S_R/X)

% RSD_{R(Hor)} = Horowitz value calculated from $2^{(1-0.5\log c)}$

where c is the concentration of the analyte as a decimal fraction (e.g. for 100% concentration c = 1)

**TABLE 1B - Cyazofamid – Summary of the statistical evaluation of the collaborative Study Data
Selected Outlier Test Results Removed**

	Cyazofamid 400 SC				
	Tech-1	Tech-2	SC-1	SC-2	SC-3
No. of Labs	14	14	15	15	15
No. of Stragglers	0	0	0	0	0
No. of Outliers	0	0	0	0	1 ^(C)
No. of Labs Retained	14	14	14	14	14
No. of Results	56	56	56	56	56
Total Mean, X (g/kg)	958.7	948.7	345.4	346.0	341.8
Repeatability standard deviation S_r	5.51	4.38	2.27	2.61	3.04
“Pure” between laboratory standard variation S_L	5.48	4.20	2.29	2.34	2.30
Reproducibility standard deviation S_R	7.77	6.07	3.23	3.50	3.82
Repeatability r	15.4	12.3	6.37	7.30	8.51
Reproducibility within lab R_L	15.3	11.8	6.42	6.54	6.45
Reproducibility between labs R	21.8	17.0	9.04	9.80	10.7
RSD_r (%)	0.58	0.46	0.66	0.75	0.89
RSD_R (%)	0.81	0.64	0.94	1.01	1.12
RSD_{R(Hor)} (%)	2.01	2.02	2.35	2.35	2.35

Limits (g/kg)

X+R	980.4	965.7	354.5	355.8	352.5
X+r	974.1	960.9	351.8	353.2	350.3
X-r	943.2	936.4	339.1	338.7	333.3
X-R	936.9	931.7	336.4	336.2	331.1

^(C) from Cochran test

^(G) from Grubbs-I test

Where :

X = average
S_r = repeatability standard deviation
S_L = “pure” between laboratory standard deviation
S_R = reproducibility standard deviation = $(S_r^2 + S_L^2)^{0.5}$
r = repeatability within-lab (2.8 S_r)
R = reproducibility between labs (2.8 S_R)
R_L = reproducibility within lab on different days (2.8 S_L)
% RSD_r = repeatability relative standard deviation (100 S_r/X)
% RSD_R = reproducibility relative standard deviation between labs (100 S_R/X)
% RSD_{R(Hor)} = Horowitz value calculated from $2^{(1-0.5\log c)}$
where c is the concentration of the analyte as a decimal fraction (e.g. for 100% concentration c = 1)

TABLE 2 - Assay Results Summary by Lab for Cyazofamid in Cyazofamid Technical, Tech-1
All values in [g/kg]

LAB	DAY 1		DAY 2		Mean	SD	Notes
	A	B	A	B			
1	953.09	948.75	954.13	955.46	952.86	2.91	
2	971.20	970.17	962.41	960.07	965.96	5.55	
3	954.61	966.24	966.45	957.55	961.21	6.04	
4							
5	960.46	962.99	965.18	969.28	964.48	3.74	
6	965.71	960.05	965.51	962.99	963.57	2.65	
7	959.48	959.09	956.68	956.96	958.05	1.44	
8	961.35	952.88	938.74	939.00	947.99	11.09	
9	957.24	959.17	957.34	956.87	957.65	1.03	
10	965.29	967.38	959.35	985.03	969.26	11.05	
11	965.99	957.54	962.58	960.99	961.77	3.51	
12	964.43	957.55	964.09	951.67	959.44	6.07	
13	952.21	952.35	946.14	950.54	950.31	2.90	
14	953.82	957.79	950.64	952.62	953.72	3.01	
15	951.85	952.00	957.50	959.10	955.11	3.74	

SD = Standard deviation

c-Cochran straggler, C-Cochran outlier, g-Grubb straggler, G-Grubb outlier

TABLE 3 - Assay Results Summary by Lab for Cyazofamid in Cyazofamid Technical, Tech-2
All values in [g/kg]

LAB	DAY 1		DAY 2		Mean	SD	Notes
	A	B	A	B			
1	944.92	942.03	954.14	949.73	947.70	5.337	
2	956.10	955.48	939.67	946.61	949.46	7.836	
3	948.34	950.75	946.36	946.93	948.10	1.956	
4							
5	946.91	945.08	955.50	951.26	949.69	4.662	
6	957.40	958.69	957.81	956.13	957.51	1.065	
7	953.92	949.61	956.06	951.08	952.67	2.885	
8	939.32	940.33	939.77	939.23	939.66	0.503	
9	953.39	949.92	950.83	950.74	951.22	1.504	
10	947.57	955.17	962.89	944.76	952.60	8.149	
11	946.82	937.24	946.96	947.38	944.60	4.913	
12	945.60	943.04	944.10	941.36	943.52	1.783	
13	952.51	952.65	952.91	954.81	953.22	1.075	
14	945.90	938.40	940.86	946.58	942.93	3.957	
15	942.90	945.45	951.59	954.90	948.71	5.506	

SD = Standard deviation

c-Cochran straggler, C-Cochran outlier, g-Grubb straggler, G-Grubb outlier

TABLE 4 - Assay Results Summary by Lab for Cyazofamid in Cyazofamid Suspension Concentrate (400 SC), Cyazofamid 400 SC-1; All values in [g/kg]

LAB	DAY 1		DAY 2		Mean	SD	Notes
	A	B	A	B			
1	342.48	343.43	345.58	346.34	344.46	1.80	C, G
2	348.30	347.50	345.73	346.11	346.91	1.20	
3	343.98	347.89	348.96	351.38	348.05	3.08	
4	347.11	347.38	347.05	346.80	347.09	0.24	
5	351.12	350.51	350.24	351.65	350.88	0.63	
6	344.97	345.02	344.06	345.13	344.80	0.49	
7	349.92	350.21	347.77	344.80	348.17	2.50	
8	338.55	340.31	344.63	346.09	342.40	3.54	
9	343.84	346.91	341.70	344.62	344.27	2.15	
10	352.22	357.86	357.60	367.77	358.86	6.48	
11	344.54	339.47	347.26	345.11	344.10	3.30	
12	341.64	342.05	343.09	343.93	342.68	1.03	
13	342.18	341.39	340.37	343.90	341.96	1.49	
14	344.43	342.21	348.25	350.83	346.43	3.85	
15	340.60	344.26	343.78	346.05	343.67	2.27	

SD = Standard deviation

c-Cochran straggler, C-Cochran outlier, g-Grubb straggler, G-Grubb outlier

TABLE 5 - Assay Results Summary by Lab for Cyazofamid in Cyazofamid Suspension Concentrate (400 SC), Cyazofamid 400 SC-2; All values in [g/kg]

LAB	DAY 1		DAY 2		Mean	SD	Notes
	A	B	A	B			
1	339.24	351.94	345.80	345.73	345.68	5.19	C, g
2	347.79	348.02	344.38	344.80	346.25	1.93	
3	347.14	345.69	351.57	353.38	349.45	3.63	
4	344.83	342.67	345.79	345.25	344.64	1.37	
5	344.73	346.64	347.16	349.20	346.93	1.84	
6	342.75	341.75	341.92	345.30	342.93	1.64	
7	350.00	350.12	351.05	349.26	350.11	0.74	
8	371.84	355.76	351.56	354.07	358.31	9.18	
9	346.10	346.91	338.89	346.86	344.69	3.88	
10	358.01	349.10	351.51	348.81	351.86	4.28	
11	341.20	344.68	346.19	346.28	344.59	2.38	
12	343.02	343.18	340.36	341.74	342.08	1.31	
13	344.15	346.02	342.57	343.53	344.07	1.46	
14	344.47	342.88	345.23	347.23	344.95	1.81	
15	344.02	344.05	347.85	344.36	345.07	1.86	

SD = Standard deviation

c-Cochran straggler, C-Cochran outlier, g-Grubb straggler, G-Grubb outlier

TABLE 6 - Assay Results Summary by Lab for Cyazofamid in Cyazofamid Suspension Concentrate (400 SC), Cyazofamid 400 SC-3; All values in [g/kg]

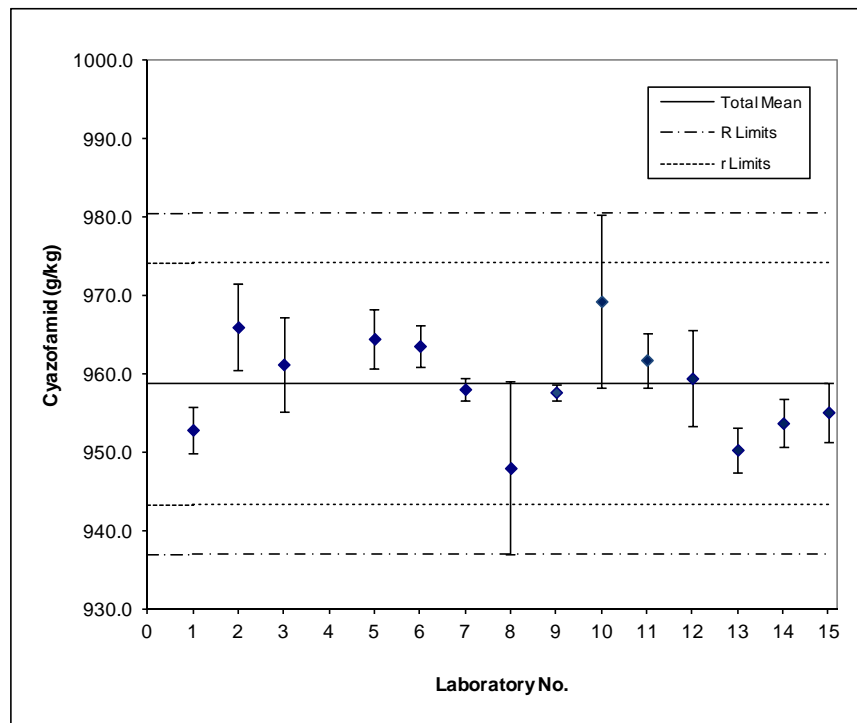
LAB	DAY 1		DAY 2		Mean	SD	Notes
	A	B	A	B			
1	336.47	341.23	343.34	345.22	341.57	3.77	
2	344.48	341.97	340.94	340.83	342.05	1.70	
3	338.90	338.34	341.36	344.49	340.77	2.80	
4	345.21	342.66	340.87	342.32	342.77	1.81	
5	342.80	340.49	345.20	343.37	342.97	1.94	
6	338.00	334.41	337.17	335.70	336.32	1.59	
7	346.63	345.87	346.97	348.34	346.95	1.03	
8	341.34	344.71	345.39	347.47	344.73	2.55	
9	339.01	340.44	348.44	329.87	339.44	7.61	C
10	364.70	360.50	359.11	378.38	365.67	8.80	C, G
11	341.80	334.47	340.38	341.33	339.50	3.40	
12	342.48	343.58	336.28	339.49	340.46	3.28	
13	340.76	342.71	340.61	342.25	341.58	1.05	
14	339.32	341.23	340.01	339.89	340.11	0.80	
15	344.95	343.19	347.31	348.32	345.94	2.32	

SD = Standard deviation

c-Cochran straggler, C-Cochran outlier, g-Grubb straggler, G-Grubb outlier

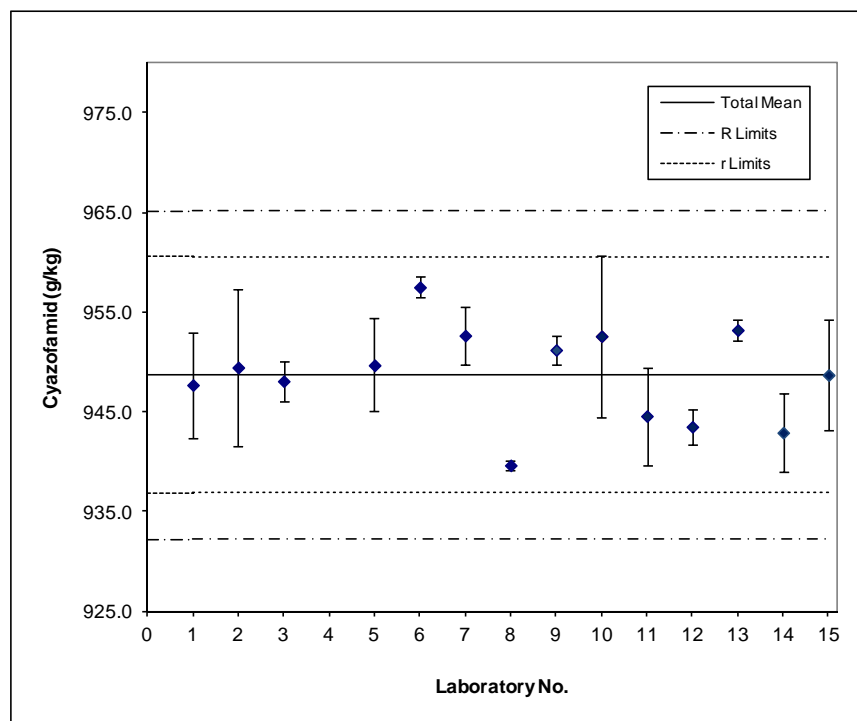
FIGURES (1-5)

FIGURE 1 - Cyazofamid in Cyazofamid Technical, Tech-1



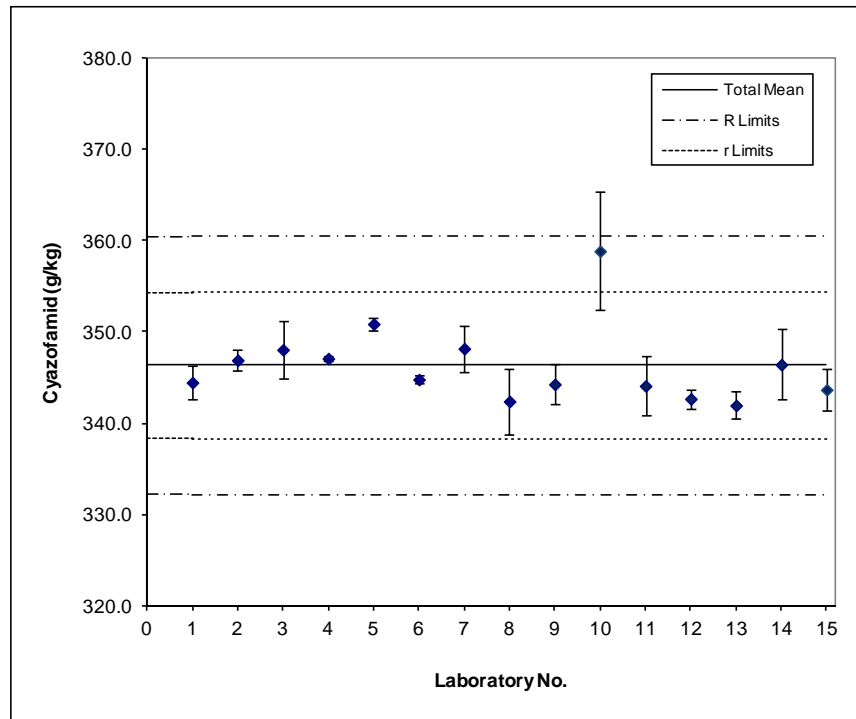
ni = 4 for all Labs

FIGURE 2 - Cyazofamid in Cyazofamid Technical, Tech-2



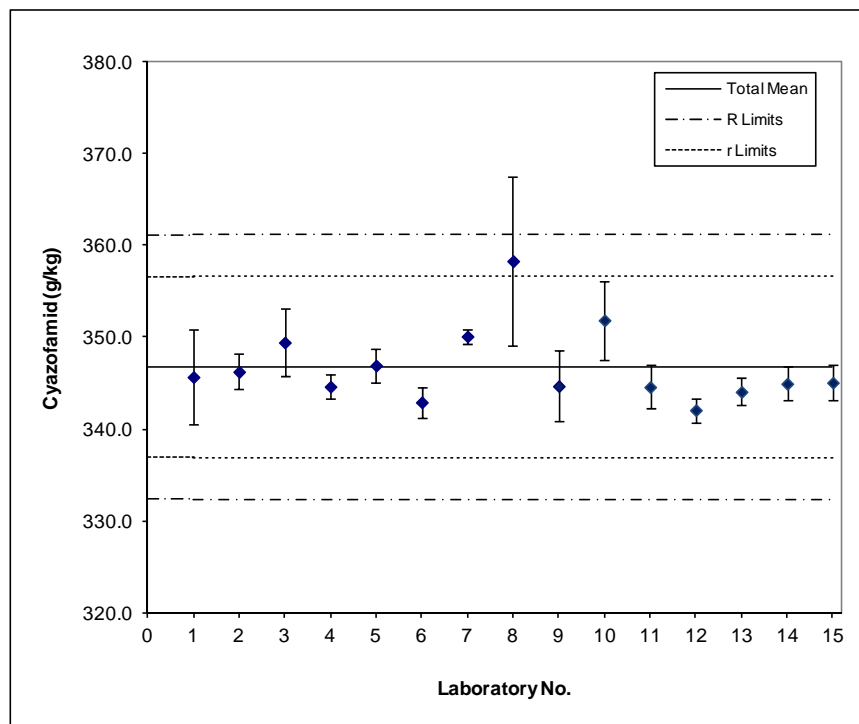
ni = 4 for all Labs

FIGURE 3 - Cyazofamid in Cyazofamid Suspension Concentrate (400 SC), Cyazofamid 400 SC-1



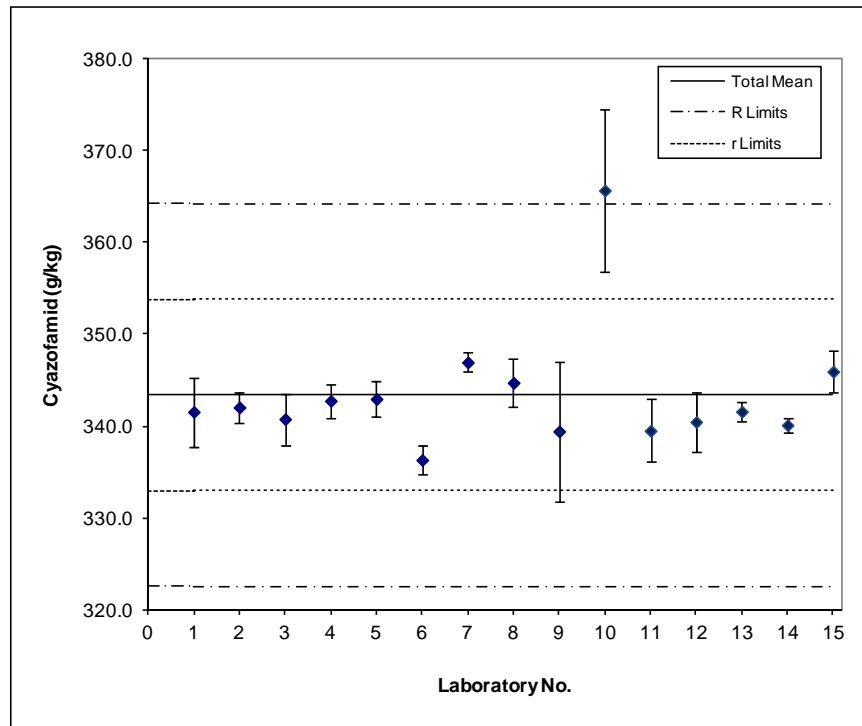
ni = 4 for all Labs

FIGURE 4 – Cyazofamid in Cyazofamid Suspension Concentrate (400 SC), Cyazofamid 400 SC-2



ni = 4 for all Labs

FIGURE 5 - Cyazofamid in Cyazofamid Suspension Concentrate (400 SC), Cyazofamid 400 SC-3



ni = 4 for all Labs